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09/258,216 02/26/99 SODERLUND

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HM12/1004

EXAMINER

ARTHUR, L

ART UNIT

PAPER NUMBER

1655

DATE MAILED:

10/04/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

813-9600

correct address

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see power of attorney  
acceptance

# Office Action Summary

Application No.  
09/258,216

Applicant(s)  
Sonderlund et al.

Examiner  
Lisa Athur

Group Art Unit  
1655



- ☐ Responsive to communication(s) filed on \_\_\_\_\_
- ☐ This action is FINAL.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claim

- ☒ Claim(s) 1-39 is/are pending in the application.
- Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- ☒ Claim(s) 1-39 is/are rejected.
- ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- ☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some\* ☒ None of the CERTIFIED copies of the priority documents have been received.
- ☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

- ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- ☒ Notice of References Cited, PTO-892
- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 3,6
- ☒ Interview Summary, PTO-413
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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1. This application is a continuation of application 08/162,376 which is now U.S. patent which is a continuation of 07/656,575, which is a continuation in part of application 07/482,005.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-19, 34-37, a method for detecting a nucleotide variation, drawn to ,  
classified in class 435, subclass 6.
- II. Claims 20-33, drawn to kits and primers, classified in class 435, subclass 6 and  
Class 536, subclass 24.33.

The inventions are distinct, each from the other because:

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the kits and primers can be used in a materially different method such as an amplification method or a detection method based upon ligation of a method for sequence.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

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During a telephone conversation with Franklin Abrahms on September 27, 2000 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-11 and 34-39. Affirmation of this election must be made by applicant in replying to this Office action. Claims 12-33 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-11, 34-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-11, 34-39 are indefinite over the recitation of "the nucleotide sequence of interest" because this phrase lacks antecedent basis.

B) Claims 1-11, 34-39 are indefinite over the recitation of "in a region disposed toward the 3' end from the defined site" because this phrase does not clearly set forth whether the primer is complementary to a region at the 3' end of the defined site, whether the primer is complementary to a region somewhere in the vicinity, i.e. "Toward" the 3' end of the defined site,

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or whether the primer hybridizes such that the 3' end of the primer on the defined site, adjacent to the defined site or near the defined site.

C) Claims 1-3 are indefinite over the recitation in step (b) of “which comprises means for detecting” because this phrase makes the claims unclear as to what comprises the means for detecting, i.e. the first or second nucleotides of the nucleoside triphosphate in the mixture.

D) Claims 2-11 are further indefinite because it does not recite a final process step which clearly relates back to the preamble . The final process step is adding a second primer but the method does not recite a step for annealing, and extending, and detecting such that a plurality of variations could be detected.

E) Claim 5 is further indefinite over the recitation of “.extending toward the 3' end of the target nucleic acid polymer from the nucleotide residue immediately adjacent to the defined site” because this phrase makes the claim unclear as to where the “region” of complementarity is located. The claim as written does not clearly set forth whether the primer is complementary to the 3' or the 5' side of the defined site.

F) Claim 10 is indefinite over the recitation of “according to claim 2 or 3” because only claim 2 recites the limitation the a plurality of nucleotide variations are to be detected.

G) Claim 11 is indefinite over the recitation of “the detectable amount of target nucleic acid polymer” because this phrase lacks antecedent basis.

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3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(g) before the applicant's invention thereof the invention was made in this country by another who had not abandoned, suppressed, or concealed it. In determining priority of invention there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

4. Claims 1, 3,5,6, 9 are rejected under 35 U.S.C. 102(a) as being anticipated by Kuppuswamy et al. (BLOOD 74(7) suppl 1 November 1989, page 254a).

Kuppuswamy et al. Teach a method for the detection of a specific nucleotide substitution at a defined site of a target nucleic acid by first amplifying a target nucleic acid, specifically exon VIII of the factor IX gene, by PCR. Then an oligonucleotide primer was hybridized to the target nucleic acid immediately flanking the 5' end of the mutation site. The primer was extended using a polymerase and a labeled nucleotide corresponding to either the wild type nucleotide or the variant nucleotide. Incorporation of the nucleotide to the 3' end of the primer was detected by agarose gel electrophoresis and autoradiography. Kuppuswamy et al. Teach that this method can be adapted to prenatal diagnosis and to other genetic diseases caused by a point mutation.

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5. Claims 1-11 are rejected under 35 U.S.C. 102(a) as being anticipated by European Patent Application EP 0332 435 A2 (hereinafter referred to as "Newton et al.).

Newton et al. teach a method for detecting point mutations by hybridizing target nucleic acid with a diagnostic primer which anneals to target nucleic acid such that the nucleotide at the point mutation is located at the 3' terminus of the primer, i.e. "the primer being complementary to the nucleotide sequence of interest in a region disposed toward the 3' end of the defined site such that when the primer is hybridized to the polymer there are no nucleotide residues between the defined site and the 3' end of the primer that are identical to the first and second nucleotide residues to be detected". The primer is then extended using a polymerase and one or more nucleotides which are complementary to the nucleotide at the 3' end of the primer. Incorporation is detected to identify the identity of the nucleotide at the defined site (abstract and page 5, lines 47-64). It is noted that the method of Newton et al. Is different from the embodiment of the claimed method limited to annealing a primer such that the 3' end of the primer is immediately adjacent to the site of a point mutation because Newton et al. teach using a annealing the primer such that the 3' terminus of the primer includes the nucleotide of the point mutation. In the method of Newton et al. Extension of the primer only occurs when the 3' terminal nucleotide is complementary to the nucleotide of the site of the point mutation. However, the claims as written broadly encompass the method of Newton et al. Because the claims do not clearly set forth that the 3' end of the primer is immediately adjacent to the site of the variation. Newton et al. Also teach that a plurality of variations can be detected using a plurality of different diagnostic primers

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(page 9, lines 25-38)(limitation of claim 2) and teach the application of the method to detection of predisposition to genetic disorders (page 9, line 31) (limitation of claim 3). Newton et al. Teach immobilization of the primer to a solid support (page 6, lines 29-32)(limitation of claim 4). Newton et al. Teach that the nucleotide used for the extension can be a deoxynucleotide (page 6, line 6) or a dideoxynucleotide (page 6, lines 12-16)(limitations of claims 5 and 7). Newton et al. Teach that the nucleotides can be labeled (page 56, lines 17-28). Newton et al. Also teach that the target can be amplified using a primer containing an attachment moiety.

6. Claims 1, 3, 5, 6, 9 are rejected under 35 U.S.C. 102(a) as being anticipated by European Patent Application EP 0 246 864 A2 (hereinafter referred to as Carr et al.).

Carr et al. Teach a method to detect specific nucleotide variations by hybridizing a first probe immediately adjacent to nucleotide to be determined such that the 3' end of the probe is immediately adjacent to the site of the point mutation. Carr et al. Further teach that a second probe is annealed to the target nucleic acid such that the 5' end of the second probe is immediately adjacent to the site of the point mutation leaving a gap of a single nucleotide between the two annealed primers. Carr et al. Then teach that the first primer is extended by a single nucleotide at its 3' end and that if the primer was extended the first and second probes are ligated in the presence of a ligase. The nucleotide variation is detected by detection of a ligated product. If a point mutation exists at the site and the complementary nucleotide was not available for extension of the primer then the two probes would not be ligated by the ligase. (Page 3, lines 23-26 and 32-



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37). It is noted that the method of Carr et al. is different from the embodiment of the claimed method limited to annealing one primer such that the 3' end of the primer is immediately adjacent to the site of a point mutation and detecting extension of the single primer as the means for detecting the nucleotide at the site of the point mutation. However, the method of Carr et al. reads on the claimed method because of the open claim language "comprising" which allows prior art methods having additional steps to read on the claim as long as the prior art has the recited steps. Carr et al. Teach the application of the method to detect predispositions to genetic diseases (page 5, lines 42-45)(limitation of claim 3).

7. Claims 1,3,4,5,7,8,9,34 are rejected under 35 U.S.C. 102(b) as being anticipated by Mundy.

Mundy disclose a method for detecting a mutation at a specific nucleotide base by hybridizing a labeled probe to target to form a hybrid such that one end of the probe is positioned adjacent to the specific base and then extending the probe by adding a nucleotide derivative such that extension will occur only if the nucleotide is complementary to the specific base. Mundy also teaches that the probe can hybridize a few bases away from the specific base to be identified and in that case deoxynucleotides are added with a modified nucleotide. Mundy also teaches using a chain terminating nucleotide to hybridize opposite the specific base Column 3) which include dideoxynucleotides (column 4). Because the claims are written with open claim language, the method of Mundy anticipates the claimed invention.

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8. Claims 1-5,7-11,34-35,37-39 are rejected under 35 U.S.C. 102(f) as being anticipated by Goelet et al.

Goelet et al. disclose a method for determining a specific nucleotide variation by hybridizing a target single stranded nucleic acid with a primer with hybridizes at its 3' end immediately adjacent to the nucleotide variation, extending the primer by a single nucleoside triphosphate which is a mixture of differently labeled dideoxynucleotides. And detecting incorporation by detecting the label on dideoxynucleotide on the end of the extended primer. Goelet et al is art against the claims of this application because the claims of this application broadly encompass the method of Goelet et al. and because the method using the dideoxynucleotides in the absence of deoxynucleotides was previously determined to be the invention of Goelet (see parent application 08/162,376).

9. Claims 1,3,5,6,9,34-39 are rejected under 35 U.S.C. 102(f) as being anticipated by Bajaj (U.S. Pat. 5,846,710). Bajaj et al. Disclose a method for detecting a specific nucleotide variation by hybridizing a single-stranded target nucleic acid with a primer which hybridizes at its 3' end flanking the nucleotide variation in the presence of only the labeled nucleotide which is complementary to the base to be determined. As written the claims of this application broadly encompass the method of Bajaj. However, the method of Bajaj was previously determined to be distinct from the method taught by Soderlund and to be the invention of Bajaj ( see parent application 08/162,376).

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10. Claims 1-1-5,7-11,34-39 are rejected under 35 U.S.C. 102(f) as being anticipated by Goelet et al (U.S. Pat 6,004,744). Goelet et al. disclose a method for determining a specific nucleotide variation by hybridizing a target single stranded nucleic acid with an immobilized or an immobilizable primer with hybridizes at its 3' end immediately adjacent to the nucleotide variation, extending the primer by a single nucleoside triphosphate which is a mixture of differently labeled dideoxynucleotides. And detecting incorporation by detecting the label on dideoxynucleotide on the end of the extended primer. Goelet et al. also teach the application of the method to the determination of a plurality of nucleotide variations . Goelet et al is art against the claims of this application because the claims of this application broadly encompass the method of Goelet et al. and because the method using the dideoxynucleotides in the absence of deoxynucleotides was previously determined to be the invention of Goelet (see parent application 08/162,376).

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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12. Claims 1-11 and 34-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-26 of U.S. Patent No. 6,013,431. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of this application and the patent contain overlapping subject matter. The claims of patent 6,013,431 are drawn to a method for determining a nucleotide variation at a defined site using a primer which hybridizes at its 3' end to the nucleotide flanking the nucleotide variation and extending in the presence of a mixture containing at least one deoxynucleotide and at least one dideoxynucleotide. The claims of the instant application are more broadly drawn hybridizing with a primer that hybridizes "toward" the nucleotide variation and extending with a mixture comprising one or more nucleotides such that at least one nucleotide is complementary to the nucleotide variation. Therefore, the claims of the instant application encompass the more specific method of patent 6,013,431.

13. No claims are allowable over the prior art.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa Arthur whose telephone number is (703) 308-3988. The examiner can normally be reached on Tuesday-Thursday from 7:00 am to 2:30 pm.

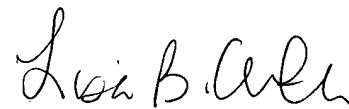
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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LISA B. ARTHUR  
PRIMARY EXAMINER  
GROUP 1800/600  
September 30, 2000